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| EXAMINER | |
|---|---|
| WANG, CHANG YU | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 12/29/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/561,014 | PAN ET AL. | |
| | Examiner | Art Unit | |
| | CHANG-YU WANG | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,6,8 and 10-44* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 17-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6, 8 and 16* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

## RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/23/09 has been entered.

### *Status of Application/Amendments/claims*

2. Applicant's amendment filed 10/23/09 is acknowledged. Claims 2-5, 7 and 9 are cancelled. Claims 1, 6, 8 and 16 are amended. Claims 1, 6, 8 and 10-44 are pending in this application. Claims 11-15 and 17-44 are withdrawn without traverse (the response filed on 5/15/08) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1, 6, 8, 10 and 16 are under examination with respect to SEQ ID NOs: 1, 3 and 36 in this office action.

4. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

5. Applicant's arguments filed on 10/23/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

### *Claim Rejections/Objections Withdrawn*

6. The rejection of claims 1, 7, 9 and 16 under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6812339 (Venter et al., issued Nov 2, 2004, priority Sep 8, 2000, as in IDS) is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 7 and 9.

The rejection of claims 1, 6-10 and 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement due to new matter is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 7 and 9.

The rejection of claims 1, 7, 9 and 16 under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6887481 (Chan et al., issued May 3, 2005, priority Dec 16, 1998) is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 7 and 9.

### *Claim Rejections/Objections Maintained*

In view of the amendment filed on 10/23/09, the following rejections are maintained.

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 8 and 16 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a purified polypeptide BNP2 comprising the amino acid sequence of SEQ ID NO: 3 and 36, does not reasonably provide

enablement for a structurally and functionally undefined polypeptide comprising an amino acid sequence having at least 85% to 95% identity to the amino acid sequence of SEQ ID NO:1 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in the scope with these claims. The rejection is maintained for the reasons made of record.

Claims 1, 6, 8 and 16 as amended are directed to a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% to 95% identity to the amino acid sequence of SEQ ID NO:1 and a pharmaceutical composition comprising the claimed polypeptides.

On p.8-9 of the response, Applicant argues that instant claims are fully enabled because the specification teaches how to make, obtain, use and obtain BNP isoforms and also provides examples 5, 6 and 10 (p.8, line 17-p. 9, lin419; p. 11, line 26-p. 12, line 21; p. 12, line 22-p. 13, line10; p. 20, line 29-p. 29, line 18). Applicant also argues that the specification provides sufficient guidance to amino acid substitutions and variants within SEQ ID NO:1 at p. 12, line 22 to p. 13, line 10. Applicant argues that a skilled artisan would know how to make and use the claimed polypeptides without undue experimentation. Applicant's arguments have been fully considered but they are persuasive.

In contrast, the specification fails to provide sufficient guidance as to how all the polypeptides comprising fragments and variants with at least 85% identity to the amino acid sequence of SEQ ID NO:1 are related to SEQ ID NO:3 or 36. As previously made

of record, the events of transcription and translation of each gene are independent from each other. The specification fails to show that the transcription and translation of the claimed polypeptides and variants comprising an amino acid sequence at least 85% identity to SEQ ID NO:1 are positively associated with SEQ ID NO:3 and 36 and thus can also be used as an diagnostic marker of heart failure.

The specification only discloses that an up-regulated expression level of SEQ ID NO:3 and 36 is found in heart tissue from heart failure patients. However, the specification does not show that the claimed variant polypeptides comprising an amino acid sequence having at least 85% identity to the amino acid sequence of SEQ ID NO:1 are also up-regulated and thus would be associated to the same disease or other diseases. The specification also fails to show that whether the claimed variant polypeptides comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1 would act in the same manner as SEQ ID NO:3 and 36 in the patients suffering from heart failure and thus can have the same utility as SEQ ID NO:3 and 36.

Thus, it is unpredictable whether all the claimed variant polypeptides comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1 are useful for a diagnostic marker of any diseases or other purposes since there is no guidance to indicate how the variant polypeptides are related to SEQ ID NO:3 or 36. It is also unpredictable which, if any other variant polypeptides would be similarly upregulated, since the regulation of a gene or a protein is not dependent on the sequence of the protein. Since the specification fails to provide sufficient guidance as to whether the variant polypeptides would be up-regulated and whether they are related to heart

diseases or other diseases, a skilled artisan cannot contemplate how to use the claimed variant polypeptides. Thus, a skilled artisan cannot contemplate how to use the claimed genus of variant polypeptides except SEQ ID NO:3 and 36.

As previously made of record, the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable what changes can be made and still maintain activity; it is also unpredictable whether the claimed undefined polypeptide variants can have the same utility as SEQ ID NO:3 or 36 as a diagnostic marker; and thus the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03

***Claim Rejections - 35 USC § 112***

8. Claims 1, 6, 8 and 16 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record.

Claims 1, 6, 8 and 16 as amended are directed to a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% to 95% identity to the amino acid sequence of SEQ ID NO:1 and a pharmaceutical composition comprising the claimed polypeptides.

On p. 9-10 of the response, Applicant argues that amended claims meet the written description requirement because the claims have been amended to recite mature BNP2 comprising at least 85% identity to SEQ ID NO:1 and the specification provides support for such amendment because the specification sets forth SEQ ID NO:36, which is a mature BNP2 that includes SEQ ID NO:1 at p. 8, line 25 to p. 9, line 7 and figure 1A. In addition, the specification teaches modifications can be made within SEQ ID NO:1 at p. 12, line 22 to p. 13, line 10 and also teaches how to determine the percent identity between two amino acid sequences at p. 9, line 20 to p. 11, line 6. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the specification only describes SEQ ID NOs: 3 and 36 and fails to teach the function of SEQ ID NO:1 or describe any other related proteins comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1. The specification fails to teach what specific common structures can or cannot be changed or included in the claimed polypeptide variants comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1 to preserve the activity of SEQ ID NOs:3 and 36. In addition, the specification also fails to teach the transcriptional and translational

relationship between the protein comprising SEQ ID NO:3 or 36 and the polypeptide variants comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1. Since the common characteristics/features of the claimed variant polypeptides are unknown, a skilled artisan can not envision the functional correlations of the claimed genus of variant polypeptides comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1 with the claimed invention. In addition, since the transcriptional and translational relationship between SEQ ID NO:3 or 36 and the claimed genus of variant polypeptides comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1 is unknown, the skilled artisan cannot envision the functional correlation of the claimed genus of polypeptide variants with SEQ ID NO:3 or 36. Note that

"A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v.Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle &Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004)."

In contrast, the specification provides an invitation for others to discover a representative number of species, or to discover what constitutes any particular portion of the structure that must be conserved, with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Thus, Applicant was not reasonably in possession of "the claimed genus of variant polypeptides comprising an amino acid sequence having at least 85% identity to SEQ ID NO:1". See MPEP 2163.

## *Conclusion*

### *Allowable Subject Matter*

9. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Claims 1, 6, 8 and 16 are rejected.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
December 08, 2009, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649